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# Decrease in the hepatitis C virus (HCV) prevalence in hemodialysis patients in Spain: effect of time, initiating HCV prevalence studies and adoption of isolation measures

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#### **Abstract**

The effectiveness of isolation measures to prevent hepatitis C virus (HCV) infection in hemodialysis units is a controversial issue. Strict adherence to the universal infection control precautions has been deemed adequate to prevent nosocomial transmission of HCV. Subsequently, however, select isolation measures, such as the clustering of HCV positive patients in a defined sector of the unit, have been adopted, specially for those units with a high HCV prevalence and when the personnel–patient ratio was such that it could involuntary favor the break of the universal precautions. In this Multicenter Spanish Study on HCV in Dialysis, the importance of both time and isolation measures led to a decrease of HCV prevalence. Time was the most important factor (although interacting with the isolation measures) and was independent of the initial HCV prevalence.

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## 1. Introduction

Hepatitis C virus (HCV) infection is considered a major Public Health problem world-wide (Jacobs et al., 2003; Kaldor et al., 2000; Patrick et al., 2001; Prati et al., 2000; Wong et al., 2000). Patients with chronic kidney diseases, and specially those in renal replacement with dialysis, have a high HCV prevalence. Hemodialysis patients are among the highest of risk groups for acquisition of HCV infection (Barril, 2000; Esteban et al., 1989; Salama et al., 2000). HCV prevalence among hemodialysis patients differs both geographically as well as among dialysis centers in the same country (Jadoul et al., 1998).

The Spanish Epidemiological Surveillance of HCV in Dialysis was created in 1991 and currently is collecting data annually on HCV prevalence and incidence as well as the adoption of isolation measures (Barril and Traver, 1995). The initial global HCV prevalence on the Spanish hemodialysis units was higher than 30%, decreasing over time to being less than 18% in 2000. By analyzing this decrease in HCV prevalence, we found that a large number of centers practiced selected isolation measures, which in the majority

of the cases consisted of dedicated health-care monitors and the provision of care in a defined sector of the unit (Barril and Traver, 2001). On the other hand, centers with no isolation measures had both a higher HCV prevalence and seroconversion rate.

The aim of this study was to analyze the contribution of different factors, such as time, adoption of isolation measures, initial HCV prevalence and number of HCV positive patients, on the decrease of HCV infection from 1993 to 1998.

## 2. Methods

Of all the centers collaborating in the Spanish Epidemiological Surveillance of HCV in Dialysis, a total of 44 of sites were selected because they provided continuous surveillance during the study period of 1993–1998. Centers were categorized according to their HCV prevalence in 1993 into one of the following quartiles:

1st quartile: 10 centers with a prevalence <17%

2nd quartile: 12 centers with a prevalence between 17 and 24%

24%

3rd quartile: 10 centers with a prevalence >24–32% 4th quartile: 12 centers with a prevalence >32%.

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Using general test linear models (repeated measures ANOVA), we analyzed as dependent variables HCV prevalence, number of HCV positive patients and seroconversion rates in hemodialysis units. For independent factors we assessed the initial HCV prevalence in 1993, isolation measures and time.

As a second step, we analyzed by repeated measures ANOVA, the impact in the decrease of HCV prevalence according to the adoption of isolation measures. For this purpose, the centers were divided as follows:

Centers that applied isolation measures since the beginning of the study (n = 27)

Centers that started isolation measures in 1994 (n = 9)Centers that never adopted isolation measures (n = 8)

### 3. Results

First, we detected a decrease in HCV prevalence from 1993 to 1998 in the four quartiles analyzed (Fig. 1). Initial HCV prevalence (P < 0.0001) and time (P < 0.0001), but not infection control isolation measures, were found to be independent variables associated with the decrease in HCV prevalence. However, there was a significant interaction between time and infection control isolation measures (P = 0.014), while the interaction between HCV prevalence in 1993 and isolation measures did not reach statistical significance (P = 0.082) (Table 1). Thus, it seems that time had the greatest impact on the decrease of HCV prevalence in hemodialysis units, but it is important to note its interaction with infection control isolation measures.

Second, the participating centers were divided into three groups according to the time of implementation of infection control isolation measures. By the Tukey's test, a decrease in HCV prevalence occurred over the entire study in each of the three groups (Fig. 2). However, only the group of centers that had no infection control isolation measures in 1993 but adopted them in 1994 showed a significant decrease annually in HCV prevalence (Table 2).

#### 4. Discussion

The spread of HCV infection in hemodialysis units is mainly due to nosocomial transmission from patient to patient (Abacioglu et al., 2000; Irish et al., 1999; Izopet et al., 1999; Kokubo et al., 2002; Olmer et al., 1997; Taskapan et al., 2001; Sanchez-Tapias, 1999). The importance of this route of transmission route is evidenced by the high HCV prevalence in some hemodialysis units and by the lower infection rate in patients on peritoneal dialysis than on hemodialysis. However, there is no consensus on the necessity of infection control isolation of HCV positive patients for several reasons. First, the infectivity of HCV is lower than that of the hepatitis B virus; second, the characteristics of the patients who required isolation remains to be defined. In this regard, the presence of anti-HCV antibodies does not necessarily imply the existence of an active HCV infection. On the contrary, some hemodialysis patients are infected with HCV infection but do not have antibodies. Detection of viral RNA by RT-PCR is the only method for confirming HCV infection but this technique is not avail-

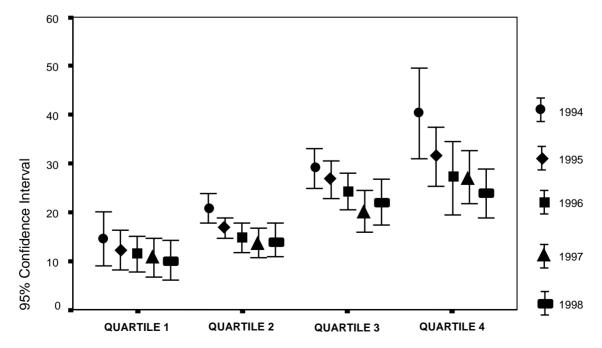


Fig. 1. Decrease in HCV prevalence in the four quartiles analyzed (repeated measures ANOVA). Quartiles are defined according to HCV prevalence in 1993: Quartile 1 (10 centers with a prevalence <17%); Quartile 2 (12 centers with a prevalence between 17 and 24%); Quartile 3 (10 centers with a prevalence >24–32%); Quartile 4 (12 centers with a prevalence >32%).

Table 1 Role (P-values) of time, isolation measures and HCV prevalence at the beginning of the study (1993) in the decrease of HCV infection in Spanish hemodialysis units

	Independent variables				
	Time		Isolation measures		HCV prevalence in 1993
Seroconversion rate	0.032		0.62		0.401
Number HCV+	< 0.0001		0.94	← 0.034	0.41
HCV prevalence	< 0.0001	← 0.014	0.44	0.082	< 0.0001

P-values boxed refer to interactions between independent variables.

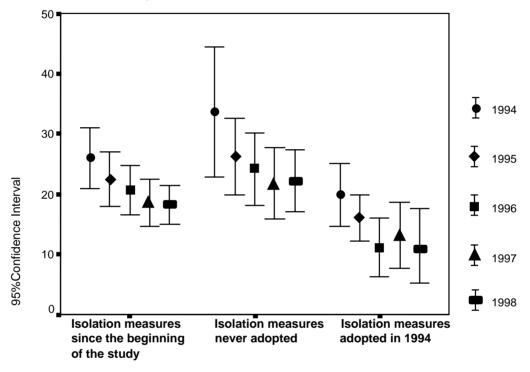


Fig. 2. Decrease in HCV prevalence according to isolation measures (repeated measures ANOVA).

able in all centers, and if available, its sensitivity may differ among centers. Furthermore, other published reports conclude that strict adherence to the universal infection control precautions is enough to fully prevent HCV nosocomial transmission (Flett et al., 1998; Gilli et al., 1995; Jadoul, 1996; Jadoul et al., 1998; Natov and Pereira, 1996; Valtuille et al., 2002). Recently, some reports have recommended the adoption of infection control isolation measures in cen-

ters with a high HCV prevalence (Arenas-Jimenez et al., 1999; Djordjevic et al., 2000; Harmankaya et al., 2002) or if the personnel unit/patient ratio in the center is lower than 28/100 (Saab, 2001).

When the Spanish Multicenter Study of Epidemiological Surveillance for HCV in Dialysis began in 1991, the global HCV prevalence in Spanish hemodialysis units was higher than 30%. Taking into account that in units with a high HCV

Table 2
Decrease of HCV prevalence in relation to isolation measures (multiple comparisons by Tukey's test)

	Never isolation measures vs. always isolation measures	Never isolation measures vs. isolation measures since 1994	Always isolation measures vs. isolation measures since 1994
1994	-7.59	-13.80*	6.20
1995	-3.76	-10.21*	6.44*
1996	-3.44	$-12.94^*$	9.50*
1997	-3.17	-8.52**	5.34
1998	-4.07	$-10.94^*$	6.87**

<sup>\*</sup> P = 0.01.

<sup>\*\*</sup> P = 0.05.

prevalence and high patient volume, universal precautions may be not always be possible to implement. Thus, we initiated isolation measures for anti-HCV positive patients. The majority of the centers have devoted health care providers for these patients in a defined areas of the unit. Only few centers had specific hemodialysis session for HCV positive patients or dialyzed them in a separate unit.

Although hemodialysis monitors can act as vertical HCV transmission vectors (Agarwal et al., 1998; Valtuille et al., 1998), their disinfection can be adequately performed (Aucella et al., 2000; Barril et al., 2000; Caramelo et al., 1994; Lombardi et al., 1995) and nowadays, vertical HCV transmission by monitors is exceptional, being the horizontal patient-to-patient transmission the most important pathway for the spread of HCV infection in hemodialysis units. So, the use of dedicated dialysis machines for infected patients in a defined area of the unit is important, provided that they are attended by devoted personnel to avoid nosocomial transmission of HCV to uninfected patients (Alfurayh et al., 2000; Saxena et al., 2003).

As demonstrated by this multicenter group, the participants have achieved a significant decrease in the seroprevalence of HCV on hemodialysis units, a prevalence now lower than 18%. When participating centers were categorized in four quartiles according to their HCV prevalence at the beginning of the study, an annual decrease in the mean HCV prevalence of the four groups was found. Analyzing different variables that could be involved in this decrease, time proved to be most important, reflecting the strict fulfillment of universal precautions. However, there was a significant interaction between time and adoption of isolation measures. Throughout the study, the highest drop in the mean HCV prevalence occurred in those centers that did not have isolation measures at the beginning of the study in 1993 but adopted them in 1994.

In summary, universal infection control precautions are the key stone in the prevention of nosocomial HCV transmission in hemodialysis units, but isolation measures, including health care monitors of infected patients and providing care in a defined section of the unit, improve the prevention results. Those hemodialysis units with a high HCV prevalence or in which there is no fulltime infection control personnel dedicated to the infected patients during the hemodialysis sessions, could have a greater risk of sero-conversion. Therefore, isolation in special units or dialyzing patients in specific sessions must be considered (Yang et al., 2003). Nevertheless, outbreaks of HCV infection may occur without a identified source of transmission, but most likely due to occasional non-fulfillment of universal precautions.

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